UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/242,977	02/26/99	WILSON J	GNVPN.019BUS

HM12/0314

HOWSON & HOWSON
SPRING HOUSE CORPORATE CENTER
PO BOX 457
SPRING HOUSE PA 19477

EXAMINER	
MARTIN, J	
ART UNIT	**PAPER NUMBER**
1632	13

DATE MAILED: 03/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/242,977	WILSON ET AL.	
	Examiner	Art Unit	
	Jill Martin	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

Applicants' Amendment filed December 27, 2000 (Paper No. 12) has been entered. Claims 7, 16, and 17 have been canceled, claims 18-21 have been amended, and claims 23-29 have been added. Claims 18-29 are pending and are under current examination.

Double Patenting

The prior obviousness-type double patenting rejection of claims 18-29 over claims 1-4 of US Patent 5,866,522 is maintained. It is acknowledged that Applicants request that this rejection be deferred until allowance.

Claim Rejections - 35 USC § 102

The Wilson Declaration filed on December 27, 2000 (Paper No. 10) under 37 CFR 1.131 has been considered but is ineffective to overcome the Gouras et al. reference because the Declaration has not been made by all the inventors of the subject matter claimed. See MPEP 715.04.

Applicants' amendment to the claim 18, removing the limitation directed to "inducible promoter" necessitated the new ground(s) rejection as follows:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 18-21 stand rejected under 35 U.S.C. 102(a) as being anticipated by Gouras et al. for the reasons advanced on pages 3-4 of the prior Office action mailed 6/21/00 (Paper No. 8).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Applicants' addition of new claims 23-25 necessitated the new ground(s) of rejection as follows:

Claims 18-22 stand and new claims 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Podsakoff et al. taken with Chiorini et al.

Applicants argue that there is no teaching or suggestion in the cited prior art for the construction of a pharmaceutical composition containing rAAV encoding apolipoprotein. See page 5, 2nd paragraph of the Amendment. While Applicants acknowledge that Podsakoff et al. teach an assay for purification of AAV away from contaminating helper virus, Applicants argue that Podsakoff et al. fail to teach or suggest the specific purification protocol of the instant specification such that the rAAV of Podsakoff et al. would be unable to result in the absence of a cytotoxic immune response directed against the cell. See page 5, paragraphs 4-6. Applicants go

on to argue that Chiorini et al. teaches transducing AAV into cell *in vitro*. See page 5, paragraph 7.

In response, it is initially noted that the claims under rejection are all directed to a product, *i.e.*, a composition comprising an rAAV comprising the gene encoding ApoE suspended in a biologically compatible carrier. The rejection of record is entirely made on the basis of the construction of a rAAV vector and not with regard to the intended use of the vector *in vivo*. The claims, as written, fail to recite any limitations which distinguish the claimed product over the prior art product. Furthermore, the limitation in new claim 25 directed to "wherein said rAAV is substantially free of contamination with a helper virus" similarly fails to distinguish the claimed composition rAAV from the prior art rAAV which is purified away from contaminating adenovirus which is all that is required by the claim. The specific purification protocol is irrelevant to the claimed product unless the protocol results in a distinguished product over the prior art product. However, as written, it is maintained that the claimed product is not distinguished from the prior art product and, thus, the 103 rejection of record is maintained.

With regard to new claim limitations directed to specific titers of rAAV, it is held that such an embodiment is sufficiently made obvious by the cited prior art of record in light of the state of the art as well as the level of skill of those in the art with regard to optimization parameters. For example, Podsakoff et al. teach the determination of effective dose range for rAAV vectors in Example 1. In particular, in Example 4, Podsakoff et al. teach i.m. injection into mice of rAAV-hEPO at 3×10^{11} vector genomes.

Applicants' addition of new claims 26-29 necessitated the new ground(s) of rejection as follows:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaplitt et al. (US Patent 6,162,796) taken with either Kashyap et al. (Ref CV of Paper No. 11) or Kashyap et al. (Circulation, 1994).

Claims 26 and 27 are directed to a method of delivering apoE to a patient for treating atherosclerosis comprising administering a rAAV to a patient, wherein apoE is expressed, particularly rAAV delivery by intramuscular administration. Claim 28 is directed to a AAV titer of 10^9. Claim 29 is directed to the same method, wherein the rAAV is substantially free of helper virus.

Kaplitt et al. teach a method for delivering rAAV vectors to and expressing genes in cardiac muscle cells or vascular endothelial cells *in vivo*, particularly for use in treating disorders of the heart or vasculature. See claims 1-36 and column 5, lines 47-54. Kaplitt et al. further indicate that it was well known in the art to obtain an AAV system, wherein helper virus could be completely eliminated leaving a helper-free AAV vector stock. See column 3, lines 15-30. While Kaplitt et al. differ from the claimed invention in that they do not specifically teach the gene

encoding human apoE, Kaplitt et al. teach that the gene of interest may encode a protein involved in cholesterol metabolism, circulation or accumulation. See column 4, lines 7-110 and claim 11. However, at the time the claimed invention was made, Kashyap et al. teach that the apoE gene was well known in the art with regard to its use for gene replacement therapeutic protocols for regression of atherosclerosis. See Abstract of both references.

Accordingly, in view of the teachings of either Kashyap et al. reference indicating that the human apoE gene was well known in the art and readily available at the time of the claimed invention, particularly toward the treatment of atherosclerosis, it would have been obvious for one of ordinary skill in the art, to modify the method of rAAV delivery of genes of interest to heart cells by selecting the gene encoding apoE. One of ordinary skill in the art would have been sufficiently motivated to select the gene encoding ApoE for use in rAAV gene delivery methods of Kaplitt et al. because Kaplitt et al. suggest the use of genes involved in cholesterol metabolism, *etc.*, and Kashyap et al. establish that the ApoE gene was well known in the art with regard to its therapeutic effect on patients with atherosclerosis.

Thus, the claimed invention as a whole is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jill Martin whose telephone number is (703)305-2147.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached at (703)305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Kay Pinkney whose telephone number is (703)305-3553.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Jill D. Martin
Patent Examiner
Art Unit 1632

KAREN M. HAUDA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600